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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,328	05/15/2002	Jay M. Meythaler	UAB-15452/22	3601

25006 7590 04/10/2007

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/049,328	MEYTHALER ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-13,15-18 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-13,15-18 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments filed August 23, 2006 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 5-13, 15-18 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebisher et al. U.S. Patent No. 5,474,547 A and Bergmann, Clinical Neuropharmacology 1985 (IDS from 1/14/04 document AB).

Aebisher et al. teach a method of alleviation of movement disorders associated with Parkinson's disease, Huntington's disease and epilepsy comprising administering GABA, GABA prodrugs and GABA potentiators via implantation of devices which would release said neuroinhibitory compounds into the brain (column 3, lines 40-67).

Aebisher et al. does not teach specifically the spastic disorders of claims 7, 8 and 26 such as spastic dystonia, spastic hypertonia, spastic disorders caused by traumatic brain injury, and idiopathic dystonia, or torsional dystonia, however, the disorders cited in Aebisher et al. such as epilepsy and Parkinson's disease are well known disorders marked by spasticity and convulsions as in the instantly claimed disorders.

Thus, it would have been made obvious to one of ordinary skill in art at the time the invention was made to treat spastic dystonia, spastic hypertonia, spastic disorders caused by traumatic brain injury, and idiopathic dystonia, or torsional dystonia with gamma-amino-butyramide motivated by the teachings of Aebisher et al. who teach administration of GABA, GABA prodrugs and GABA potentiators for treatment of disorders of spasticity such as Parkinson's and epilepsy.

Aebisher et al. does not specifically teach Gamma aminobutyramide.

Bergmann teaches that Progabide, a prodrug of GABA is metabolized to *a* chloro-4'phenyl fluoro-5 hydroxy-2-benzylidene amino 4 butanoate sodium, and then to **GABAmide** (gamma aminobutyramide) which appears in the circulation and in the brain in a few minutes after administration (see pages 13-14). The compound is employed to treat spasticity (page 19) epilepsy and convulsions (pages 17-19) and Parkinson's disease (spastic hypertonia) (pages 20-21). Although it is not specifically recited, GABAmide is necessarily present because of the administration of progabide for the treatment of seizure disorders,and the inevitable metabolism of progabide to GABAmide as stated above.

Regarding claims 2, 3, 5, 6, 13, 15, 16 and 17 drawn to intrathecal administration, intraventricular administration, by an implantable pump and a spinal catheter for delivery of gamma aminobutyramide, Aebisher et al. teach an implantable pump for administration of GABA and its prodrugs and potentiators. Bergmann teaches that Progabide, a prodrug of GABA is metabolized **GABAmide** (gamma aminobutyramide), and it appears in the circulation and in the brain in a few minutes

after administration (see pages 13-14). Thus would have been made obvious to one of ordinary skill in art at the time it was made to administer prodrugs/derivatives of gamma aminobutyramide intrathecally, intraventricularly, by an implantable pump or spinal catheter motivated by the teaching of Aebisher et al. who administers GABA by an implantable pump in the brain and the teaching of Bergmann that gastric-resistant formulations of progabide have been shown to result in incomplete absorption and lower serum levels. As anyone of ordinary skill in the art will appreciate modes of administration are art-recognized result-effective variables and it would have been obvious to one of ordinary skill in the art to optimize them from the teachings of the prior art. Since the gastric-resistant formulations result in incomplete absorption, it would have been obvious to administer the compound by parenteral means, such as intraventricularly and intrathecally. Further evidence of obviousness would flow from the teaching of Aebisher et al. who teach administration of GABA by an implantable pump in the brain wherein the GABA, GABA prodrugs or GABA potentiators would metabolize to GABAmide in the ventricles of the brain, this resulting in intraventricular administration. Regarding the intrathecal administration, intrathecal administration means administering parenterally to the subarachnoid space. The subarachnoid space is the compartment within the spinal column that contains the cerebrospinal fluid (CSF). CSF is produced in the ventricular system of the brain. It communicates freely with the subarachnoid space via the foramina of Luschka and Magendie near the brainstem. Thus would have been made obvious to one of ordinary skill in art at the time it was made to administer prodrugs/derivatives of gamma aminobutyramide intrathecally,

intraventricularly, by an implantable pump or spinal catheter motivated by the teaching of Aebisher et al. who administers GABA by an implantable pump in the brain and the teaching of Bergmann that gastric-resistant formulations of progabide have been shown to result in incomplete absorption and lower serum levels. Since the gastric-resistant formulations result in incomplete absorption, it would have been obvious to administer the compound by parenteral means, such as intraventricularly and intrathecally since all would result in CSF administration as in Aebisher et al.

Response to Arguments

Applicant has amended claims 1, 11, 18 and 26 to "consisting of" gamma-aminobutyramide or a pharmaceutically acceptable salt, however, the administration step still contains "comprising language". The claim language *comprising* leaves the claim open for the inclusion of unspecified ingredients, even in major amounts. Thus the claims do not exclude the administration of, for example progabide, which subsequently metabolizes to gamma-aminobutyramide.

Regarding the side effects noted in the Ferrandes et al. article appended to the November 23, 2005 response, Applicant appears to confuse the requirements for patentability with those of receiving FDA approval. See e.g. In re Anthony, 414 F.2d 1383, 1395, 162 USPQ 594, 604 (CCPA 1969). Consequently, this argument does not raise an issue of material fact.

In *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373 [67 USPQ2d 1664] (Fed. Cir. 2003), the claims at issue covered a metabolite of the drug Loratadine,

i.e., "the compound formed in the patient's body upon ingestion of [that] pharmaceutical." *Id.* at 1375. The board held that these claims were anticipated by an earlier patent for the drug itself. *Id.* at 1382. This conclusion was based in part on the assumption that ingesting the earlier claimed pharmaceutical would create the metabolite and thus infringe the metabolite patent. *Id.* at 1380. In the instant case, Aebisher et al. teach a method of alleviation of movement disorders associated with Parkinson's disease, Huntington's disease and epilepsy comprising administering GABA, GABA prodrugs and GABA potentiators, such as Progabide, which, when ingested creates the metabolite gamma aminobutyramide in the body of the patient, thus alleviating the very same movement disorders. Regarding the method of administration, as anyone of ordinary skill in the art will appreciate modes of administration are art-recognized result-effective variables and it would have been obvious to one of ordinary skill in the art to optimize them from the teachings of the prior art. Since the gastric-resistant formulations result in incomplete absorption, it would have been obvious to administer the compound by parenteral means, such as intraventricularly and intrathecally. Further evidence of obviousness would flow from the teaching of Aebisher et al. who teach administration of GABA by an implantable pump in the brain wherein the GABA, GABA prodrugs or GABA potentiators would metabolize to GABAmide in the ventricles of the brain, this resulting in intraventricular administration. Regarding the intrathecal administration, intrathecal administration means administering parenterally to the subarachnoid space. The subarachnoid space is the compartment within the spinal column that contains the cerebrospinal fluid (CSF).

CSF is produced in the ventricular system of the brain. It communicates freely with the subarachnoid space via the foramina of Luschka and Magendie near the brainstem.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

March 28, 2007

Ardin H Marschel 3/31/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER